evidence of efficacy. That is, if you take the categories "probably effective," "possibly effective," "ineffective." Dr. Simmons, in his December 29 speech [1] said:

> Of the 16,000 therapeutic claims evaluated by the panels, approximately 11,000, or 70 percent, were found to lack adequate evidence of efficacy.

Do you have a reconciliation of those two figures?

Dr. EDWARDS. I suspect he was including in that category the "effective but" drugs. You see, on some of these drugs that were categorized by the Academy as "effective but," the staff of the FDA made an interpretation of their comments and placed them into the "possibly," "probably," "ineffective" or "effective" categories.

Senator NELSON. I see.

Dr. EDWARDS. So, I think that would account for the discrepancy in numbers.

Senator NELSON. Thank you.

Dr. EDWARDS. Moving on to these two problem areas, combination of drugs account for about 50 percent of the products involved in the National Academy of Sciences reviews. Though the NAS–NRC panels in general ruled against fixed dose combination drugs, 40 percent of America's best selling drugs are fixed dose combinations. It has been estimated that 40 to 50 percent of the prescriptions call for drugs in fixed combination dosage form. The limitations of effectiveness, the limitations of rational use and the built-in hazards that attend the use of some fixed combination dosage forms have long been recognized. They are discussed in the NAS–NRC report, they are discussed in resolutions by the AMA's Council on Drugs, in testimony before this committee, and certainly by many experts in the medical literature.

I would, however, like to make it abundantly clear that FDA is not against all fixed dose combinations. Our problem is to develop and to implement a reasonable policy for dealing with fixed dose combination drugs to make rational prescribing possible.

Senator NELSON. Is it not correct, however, that the NAS–NRC position thus far on fixed combination dosage forms is that the fixed combination that they have endorsed have been an exception to the rule?

Dr. EDWARDS. That is correct.

Essentially, our problem is to allow the marketing of those fixed combination drugs which fill a need among that patient population requiring concomitant therapy with multiple drug ingredients at the particular dosage levels offered. This must be done without permitting the marketing of irrational fixed dose combinations intended for patients who may have a condition amenable to treatment by one or more of the components but who has no need for the others. Certainly, the hazards of unneeded drugs are all too well known to require any extended discussion today.

Mr. GORDON. Dr. Edwards, what is your new policy with respect to combinations and what do you hope to accomplish by it?

Dr. EDWARDS. We are in the process of developing guidelines, if you will, as to what we consider an adequate combination drug. We will probably be publishing these in the Federal Register within the

[1] See pp. 8426–8443.